STIC SEARCH 10/771652

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09-18-06

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STRUCTURE FILE UPDATES: 17 SEP 2006 HIGHEST RN 907180-17-0
DICTIONARY FILE UPDATES: 17 SEP 2006 HIGHEST RN 907180-17-0

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d l15 ide can tot

L15 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
RN 731002-35-0 REGISTRY
ED Entered STN: 23 Aug 2004
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FS PROTEIN SEQUENCE; STEREOSEARCH
MF **C54 H78 N12 O25 . 2 C2 H F3 O2**
SR CA
LC STN Files: CA, CAPLUS, CASREACT

PRIORITY 04/25/2001

RELATED SEQUENCES AVAILABLE WITH SEQLINK

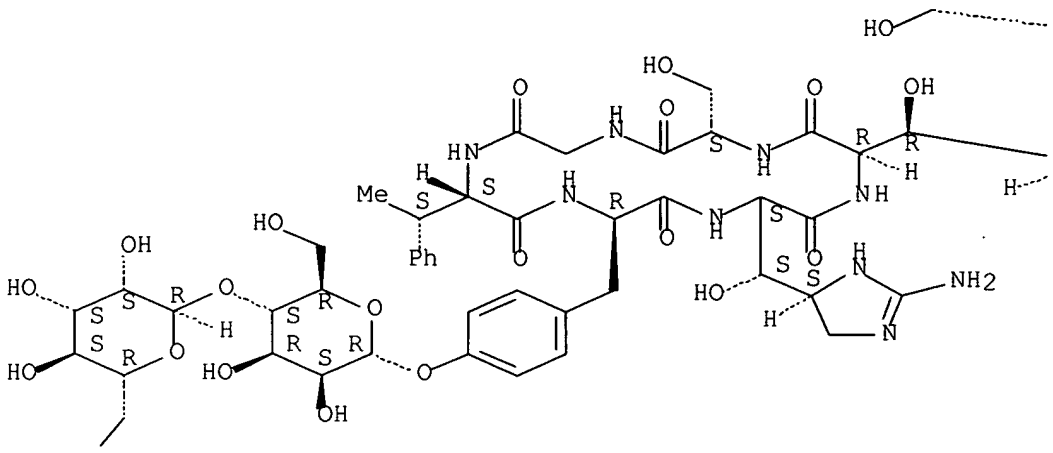
CM 1

CRN 464875-69-2
CMF C54 H78 N12 O25

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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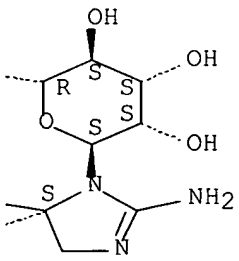

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CRN 76-05-1
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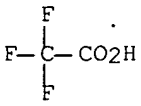


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:6727

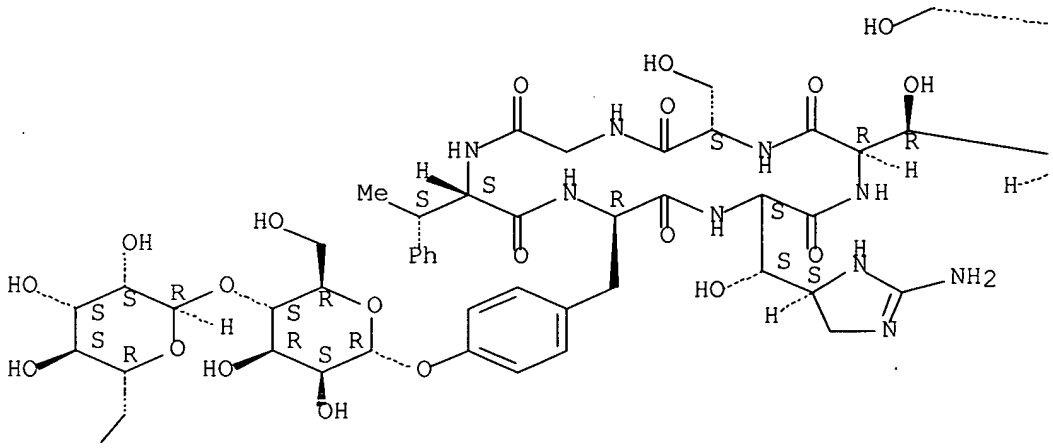
REFERENCE 2: 141:157463

L15 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
RN 609337-21-5 REGISTRY
ED Entered STN: 27 Oct 2003
CN Cyclo[glycyl-(βS)-β-methyl-L-phenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)-D-tyrosyl-(3S)-3-[(4S)-2-amino-4,5-dihydro-1H-imidazol-4-yl]-L-seryl-(3R)-3-[(5S)-2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl]-D-seryl-L-seryl], dihydrochloride (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF **C54 H78 N12 O25 . 2 Cl H**
SR CA
LC STN Files: CA, CAPLUS, CASREACT
CRN (464875-69-2)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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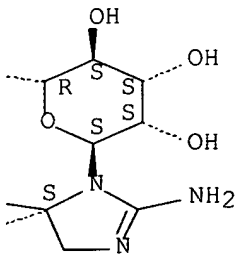

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REFERENCE 1: 141:157463

REFERENCE 2: 139:292472

L15 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
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ED Entered STN: 22 Nov 2002
CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
DR 474331-48-1
MF **C54 H78 N12 O25 . 2 C2 H F3 O2**
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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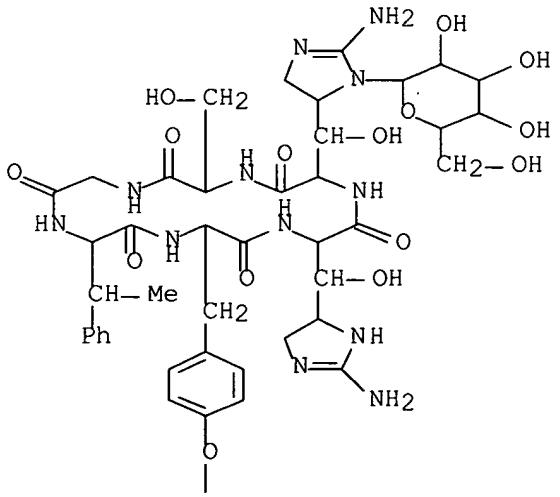
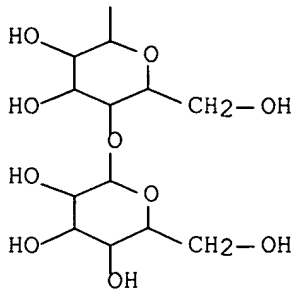
CRN 474327-82-7
CMF C54 H78 N12 O25

RELATED SEQUENCES AVAILABLE WITH SEQLINK





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CRN 76-05-1
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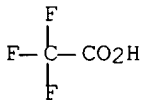

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REFERENCE 1: 137:338136

REFERENCE 2: 137:336791

L15 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
RN 474328-87-5 REGISTRY
ED Entered STN: 22 Nov 2002
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FS PROTEIN SEQUENCE
MF **C54 H78 N12 O25 . 2 Cl H**
SR CA
LC STN Files: CA, CAPLUS
CRN (474327-82-7)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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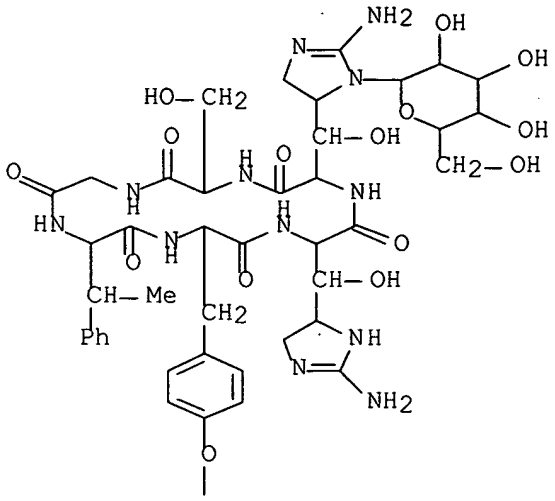

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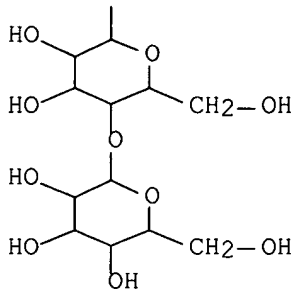

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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

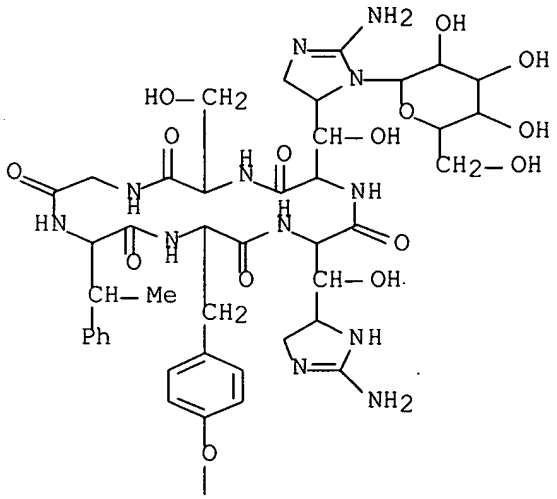
REFERENCE 1: 137:338136

REFERENCE 2: 137:336791

L15 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
RN 474327-82-7 REGISTRY
ED Entered STN: 22 Nov 2002
CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF **C54 H78 N12 O25**
CI COM
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

PAGE 1-A



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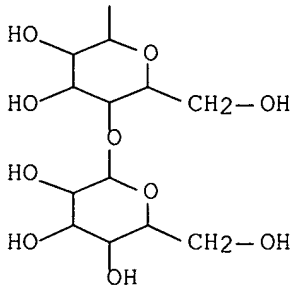

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:338136

REFERENCE 2: 137:336791

L15 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
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ED Entered STN: 15 Nov 2002
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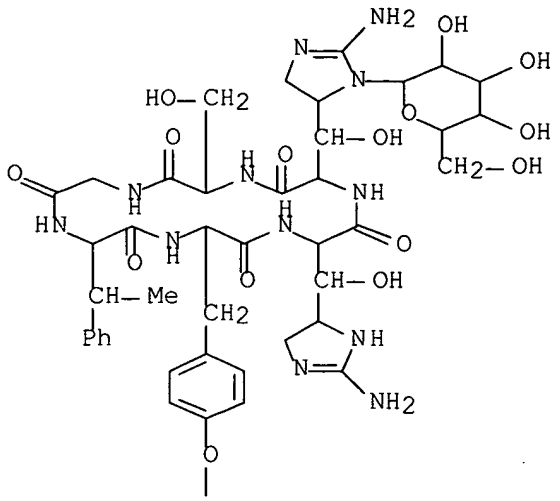
OTHER NAMES:

CN AC 98-1
FS PROTEIN SEQUENCE; STEREOSEARCH
MF **C54 H78 N12 O25**
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

PAGE 1-A



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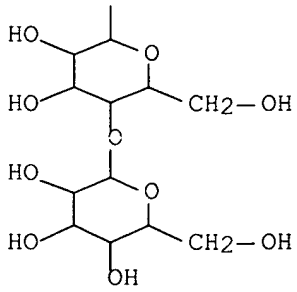

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REFERENCE 1: 141:136208

REFERENCE 2: 139:303798

REFERENCE 3: 137:329405

L15 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
RN 464875-69-2 REGISTRY
ED Entered STN: 24 Oct 2002
CN Cyclo[glycyl-(βS)-β-methyl-L-phenylalanyl-O-(4-O-α-D-

mannopyranosyl-α-D-mannopyranosyl)-D-tyrosyl-(3S)-3-[(4S)-2-amino-4,5-dihydro-1H-imidazol-4-yl]-L-seryl-(3R)-3-[(5S)-2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl]-D-seryl-L-seryl] (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Mannopeptimycin α

FS PROTEIN SEQUENCE; STEREOSEARCH

MF **C54 H78 N12 O25**

CI COM

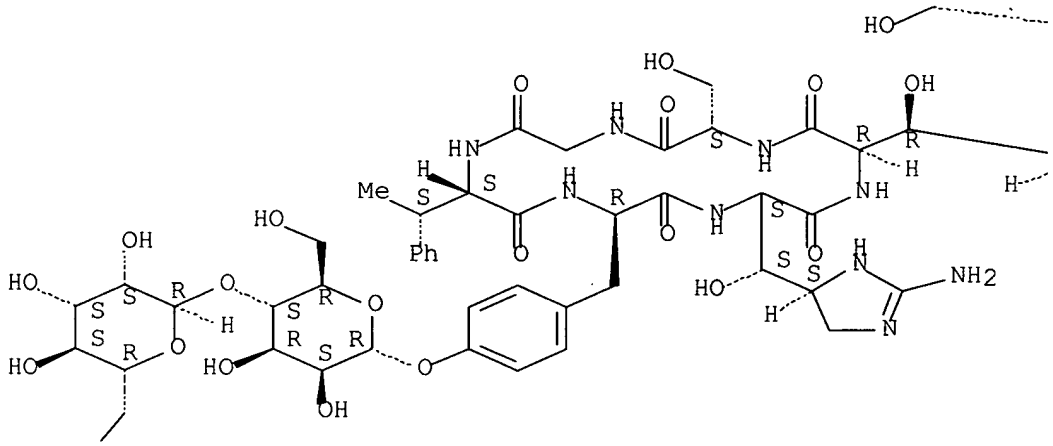
SR CA

LC STN Files: CA, CAPLUS, CASREACT

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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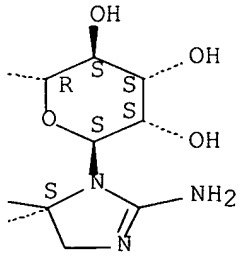

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:140899

REFERENCE 2: 144:407856

REFERENCE 3: 143:225639

REFERENCE 4: 141:243814

REFERENCE 5: 141:157463

REFERENCE 6: 140:236081

REFERENCE 7: 139:292472

REFERENCE 8: 139:127398

REFERENCE 9: 138:234668

REFERENCE 10: 137:275446

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FILE COVERS 1907 - 18 Sep 2006 VOL 145 ISS 13
FILE LAST UPDATED: 17 Sep 2006 (20060917/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l23 bib abs hitstr retable tot

L23 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:832983 HCAPLUS Full-text
DN 137:336791
TI Preparation of glycopeptide antibiotics
IN Abbanat, Darren Robert; Bailey, Arthur Emery; Bernan, Valerie Sue; Greenstein, Michael; Lotvin, Jason Arnold; Ruppen, Mark Edward;

Sutherland, Alan Gordon; **He, Haiyin**

PA American Cyanamid Company, USA

SO PCT Int. Appl., 515 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	US 2003087812	A1	20030508	US 2002-131890	20020425 <--
	US 6914045	B2	20050705		
	US 2003092610	A1	20030515	US 2002-131847	20020425 <--
	US 6964860	B2	20051115		
	EP 1390521	A1	20040225	EP 2002-764346	20020425 <--
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	US 2005288221	A1	20051229	US 2005-116149	20050427 <--
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	US 2002-131847	A3	20020425		
	US 2002-132012	A3	20020425 <--		
	WO 2002-US13108	W	20020425 <--		

OS MARPAT 137:336791

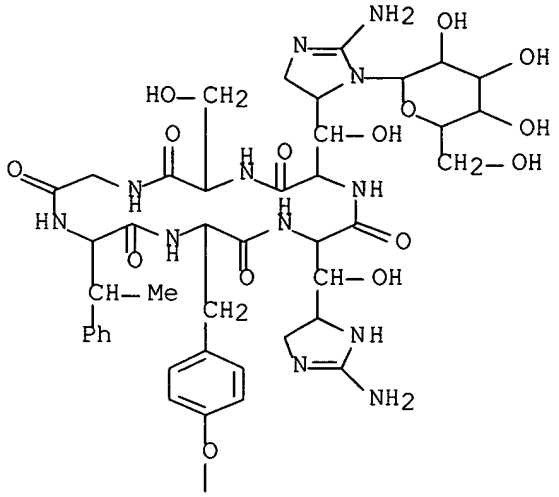
AB The invention provides glycopeptide antibiotics and their derivs. prepared by fermentation of Streptomyces hygroscopicus strains and modified by organic transformation, biochem. transformation and biotransformation. These compds. are useful as antibiotic agents against gram pos. and neg. bacteria.

IT **474327-82-7P**
RL: BCP (Biochemical process); BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of glycopeptide antibiotics)

RN 474327-82-7 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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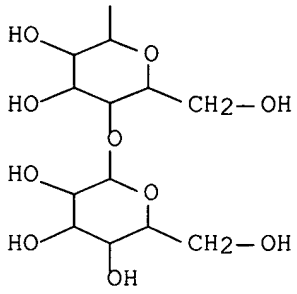


IT **474328-98-8P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of glycopeptide antibiotics)

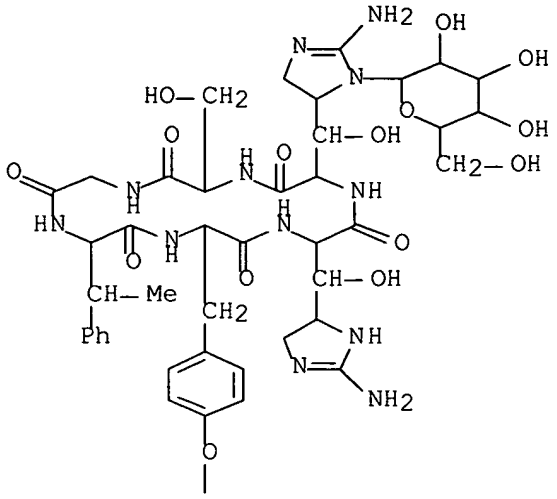
RN 474328-98-8 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 474327-82-7
CMF C54 H78 N12 O25

PAGE 1-A



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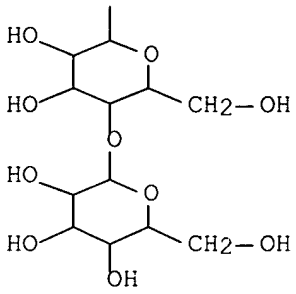

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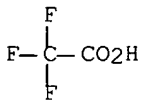
CRN 76-05-1
CMF C2 H F3 O2

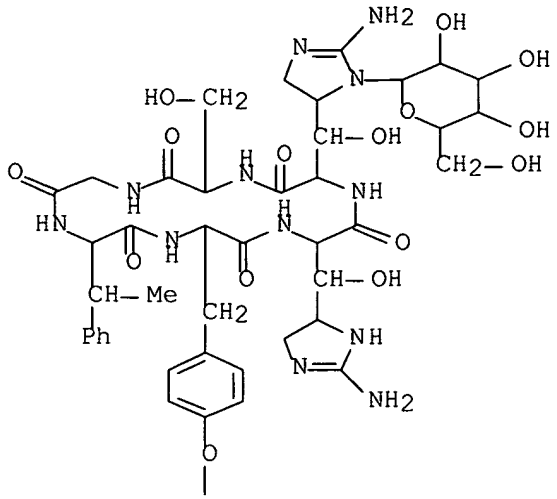


IT **474328-87-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of glycopeptide antibiotics)

RN 474328-87-5 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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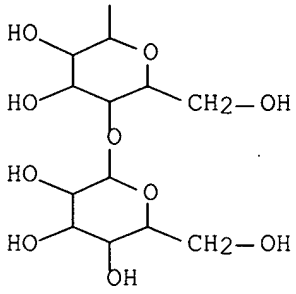

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IT **474328-98-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of glycopeptide antibiotics)

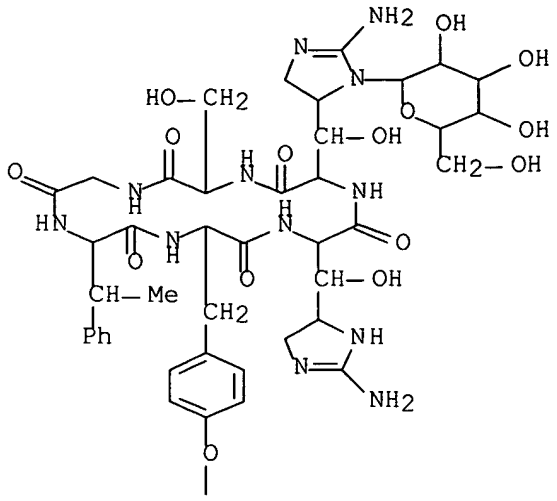
RN 474328-98-8 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 474327-82-7
CMF C54 H78 N12 O25

PAGE 1-A



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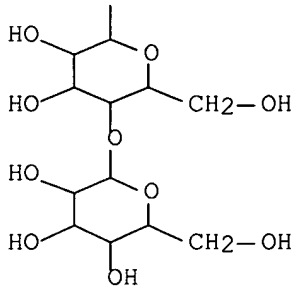

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CRN 76-05-1
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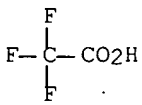

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
de Voe	1970			US 3495004	HCAPLUS

L23 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:832646 HCAPLUS Full-text

DN 137:329405
TI Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5
IN **Carter, Guy Thomas; He, Haiyin**
PA American Cyanamid Company, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002085403	A1	20021031	WO 2002-US13073	20020425 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	US 2003054508	A1	20030320	US 2002-132012	20020425 <--
	US 6713448	B2	20040330		
	US 2003087812	A1	20030508	US 2002-131890	20020425 <--
	US 6914045	B2	20050705		
	US 2003092610	A1	20030515	US 2002-131847	20020425 <--
	US 6964860	B2	20051115		
	EP 1399176	A1	20040324	EP 2002-739179	20020425 <--
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	US 2005288221	A1	20051229	US 2005-116149	20050427 <--
PRAI	US 2001-286249P	P	20010425 <--		
	US 2001-286244P	P	20010425 <--		
	US 2001-286396P	P	20010425 <--		
	US 2002-131847	A3	20020425		
	US 2002-132012	A3	20020425 <--		
	WO 2002-US13073	W	20020425		

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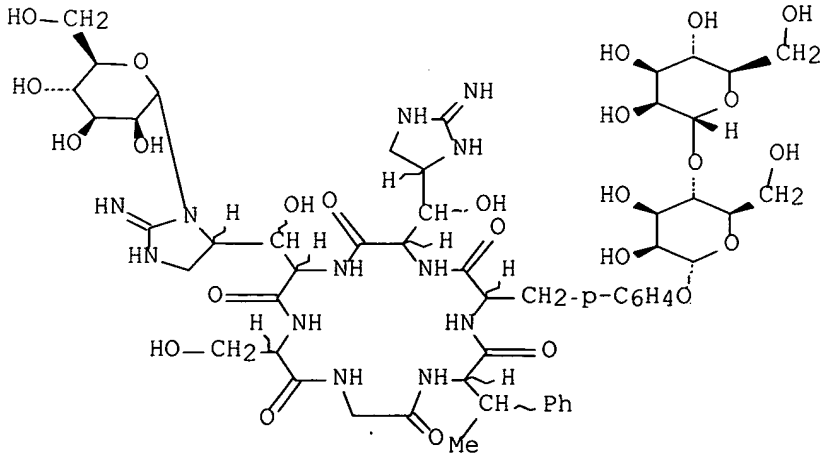


I

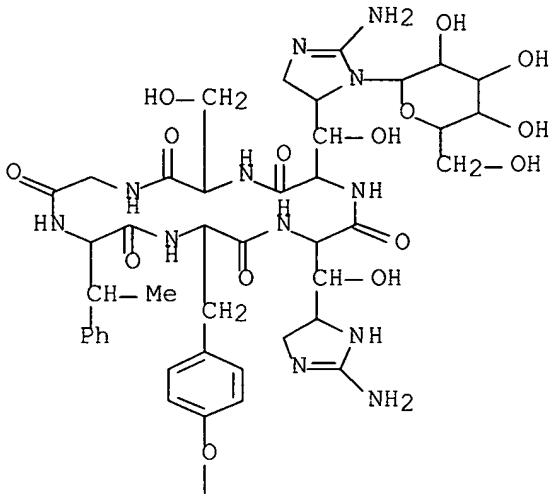
AB The invention provides new substantially pure antibiotics designated **AC-98-1** (I), AC-98-2, AC-98-3, AC-98-4 and AC-98-5 derived from the microorganism Streptomyces hygroscopicus. The mixture was prepared from a fermentation and the compds. isolated and characterized and their antibacterial activity determined

IT **473722-21-3P, AC 98-1**
RL: BMF (Bioindustrial manufacture); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substantially pure AC-98 glycopeptide antibiotics)

RN 473722-21-3 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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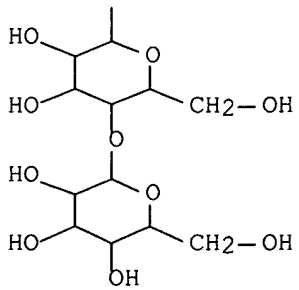

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File

Bossi	1999			US 5939523 A	HCAPLUS
de Voe	1970			US 3495004 A	HCAPLUS
Malabarba	1997			US 5648456 A	HCAPLUS

L23 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:832574 HCAPLUS Full-text
DN 137:338136
TI Preparation of glycopeptide antibiotics
IN Abbanat, Darren Robert; Bernan, Valerie Sue; Dushin, Russell George; Greenstein, Michael; **He, Haiyin**; Lang, Stanley Albert; Newman, Howard; Sakya, Subas; Sum, Phaik-Eng; Sutherland, Alan Gordon; Wang, Ting-Zhong; Ruppen, Mark Edward; Bailey, Arthur Emery; Chi, Ping; Shen, Bo; Kong, Fangming; Lotvin, Jason Arnold
PA American Cyanamid Company, USA
SO PCT Int. Appl., 548 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002085307	A2	20021031	WO 2002-US13120	20020425 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	AU 2002303480	A1	20021105	AU 2002-303480	20020425 <--
	US 2003054508	A1	20030320	US 2002-132012	20020425 <--
	US 6713448	B2	20040330		
	US 2003087812	A1	20030508	US 2002-131890	20020425 <--
	US 6914045	B2	20050705		
	US 2003092610	A1	20030515	US 2002-131847	20020425 <--
	US 6964860	B2	20051115		
	EP 1390056	A2	20040225	EP 2002-731505	20020425 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004158035	A1	20040812	US 2004-771652	20040204 <--
	US 2005288221	A1	20051229	US 2005-116149	20050427 <--
PRAI	US 2001-286244P	P	20010425	<--	
	US 2001-286249P	P	20010425	<--	
	US 2001-286396P	P	20010425	<--	
	US 2002-131847	A3	20020425		
	US 2002-132012	A3	20020425	<--	
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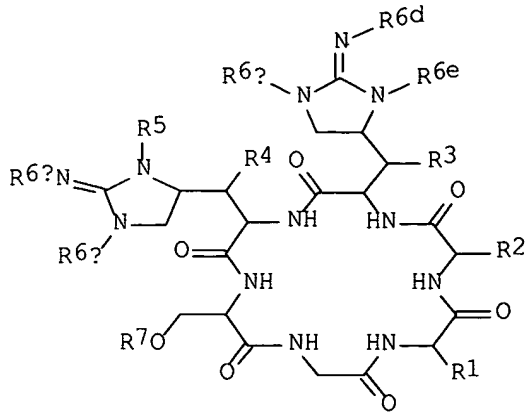
OS MARPAT 137:338136
GI



I

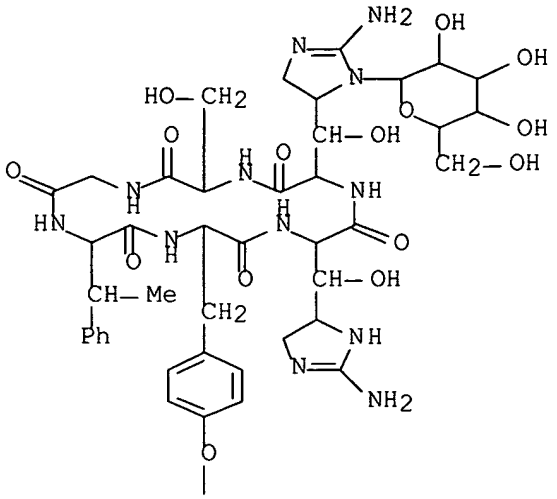
AB Glycopeptide antibiotics I [R1 = 1-phenylethyl, 1-(halophenyl)ethyl, benzyl, 1-(2-thienyl)ethyl, 1-cyclohexylethyl, cyclohexylmethyl, phenyl; R2 = CH2C6H2R2b(OR2a)R2c-3,4,5 (R2a, R2b, R2c = H, (cyclo)alkyl, etc.), 4-R2aO-substituted cyclohexylmethyl, cyclohexylmethyl, 2-substituted 5-benzoxazolyl or 5-benzofuranyl; R3, R4 = H, OH, a silyl or acyl group; R5, R6a-R6e = H, (cyclo)alkyl, alkenyl, alkynyl, acyl, 2- or 4-nitrophenyl, certain heterocyclic groups; R7 = H, (cyclo)alkyl, alkenyl, alkynyl, a silyl or acyl group (with provisos)] or their pharmaceutically-acceptable salts were prepared and assayed for biol. activity. Thus, cyclo[3-cyclohexyl-2-aminobutanoyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-iminoimidazolidin-4-yl)seryl-3-(3-hexopyranosyl-2-iminoimidazolidin-4-yl)serylserylglycyl] (claimed compound) was prepared and showed MIC = 32 and 4 μg/mL for inhibition of Staphylococcus aureus (GC 1131) and Coagulase Neg. Staphylococcus (GC 4549), resp.

IT **474327-82-7P**
RL: BCP (Biochemical process); BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of glycopeptide antibiotics)

RN 474327-82-7 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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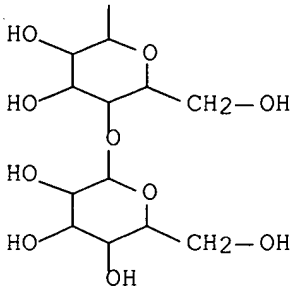

IT **474328-98-8P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of glycopeptide antibiotics)

RN 474328-98-8 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

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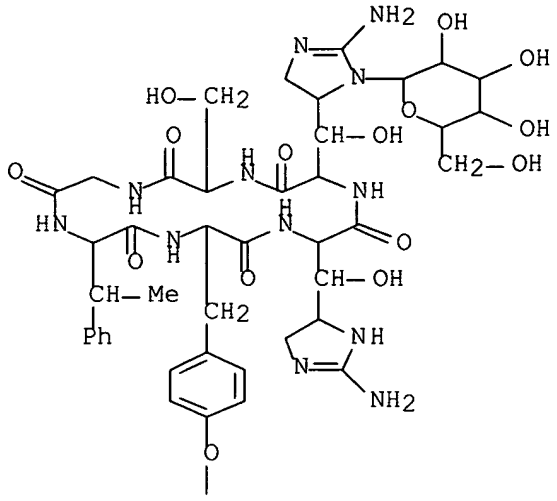
CRN 474327-82-7
CMF C54 H78 N12 O25

PAGE 1-A



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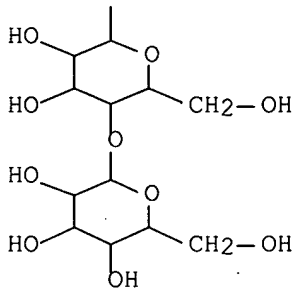

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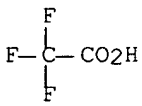
CRN 76-05-1
CMF C2 H F3 O2

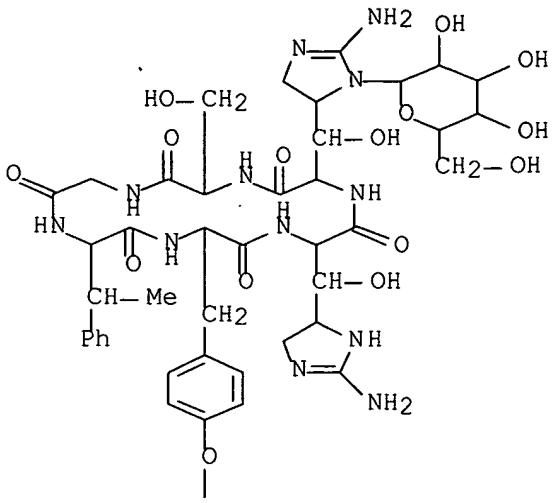


IT **474328-87-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of glycopeptide antibiotics)

RN 474328-87-5 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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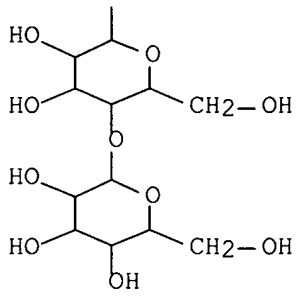

●2 HCl

IT **474328-98-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of glycopeptide antibiotics)

RN 474328-98-8 HCAPLUS

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-hexopyranosylhexopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-1-hexopyranosyl-4,5-dihydro-1H-imidazol-5-yl)serylseryl], bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

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CRN 474327-82-7
CMF C54 H78 N12 O25

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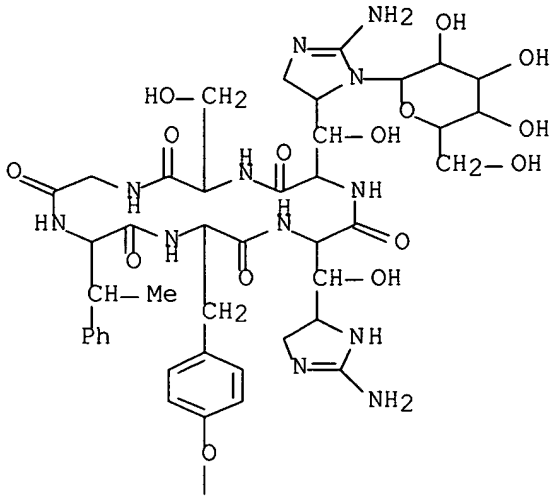

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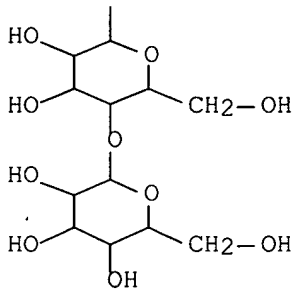

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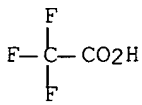

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 14 Sep 2006 (20060914/PD)
FILE LAST UPDATED: 14 Sep 2006 (20060914/ED)

HIGHEST GRANTED PATENT NUMBER: US7107620
HIGHEST APPLICATION PUBLICATION NUMBER: US2006206975
CA INDEXING IS CURRENT THROUGH 12 Sep 2006 (20060912/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 14 Sep 2006 (20060914/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

=> d l26 bib abs kwic hitstr tot

L26 ANSWER 1 OF 5 USPATFULL on STN
AN 2005:331236 USPATFULL Full-text
TI Glycopeptide antibiotics
IN Lotvin, Jason Arnold, Union, NJ, UNITED STATES
Ruppen, Mark Edward, Garnerville, NY, UNITED STATES
PA Wyeth Holdings Corporation, Madison, NJ, UNITED STATES, 07940 (U.S. corporation)
PI US 2005288221 A1 20051229
AI US 2005-116149 A1 20050427 (11)
RLI Division of Ser. No. US 2002-131847, filed on 25 Apr 2002, PENDING
PRAI US 2001-286396P 20010425 (60) <--
US 2001-286244P 20010425 (60) <--
US 2001-286249P 20010425 (60) <--
DT Utility
FS APPLICATION
LREP WYETH, PATENT LAW GROUP, 5 GIRALDA FARMS, MADISON, NJ, 07940, US
CLMN Number of Claims: 18
ECL Exemplary Claim: 1-88
DRWN No Drawings
LN.CNT 17141
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides compounds of formula ##STR1## Wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6a, R.sup.6b, R.sup.6c, R.sup.6d, R.sup.6e and R.sup.7 are defined in the specification. These compounds are useful as antibiotic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PRAI US 2001-286396P 20010425 (60) <--
PRAI US 2001-286244P 20010425 (60) <--
PRAI US 2001-286249P 20010425 (60) <--
DETD . . . strain LL4600, the complex may also be prepared. Further separation of the complex of antibiotics by HPLC into individual components **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 and determination of the chemical structures by spectroscopy is described in copending provisional patent application. . . filed Apr. 25, 2001. The structures of the individual components are shown below.

R.sup.1 R.sup.2
R.sup.3 R.sup.4 R.sup.5

AC- 98-1 ##STR113## ##STR114##
OH OH ##STR115##
AC- 98-2 ##STR116## ##STR117##
OH OH ##STR118##
AC- 98-3 ##STR119## ##STR120##

OH OH ##STR121##

AC-. . .

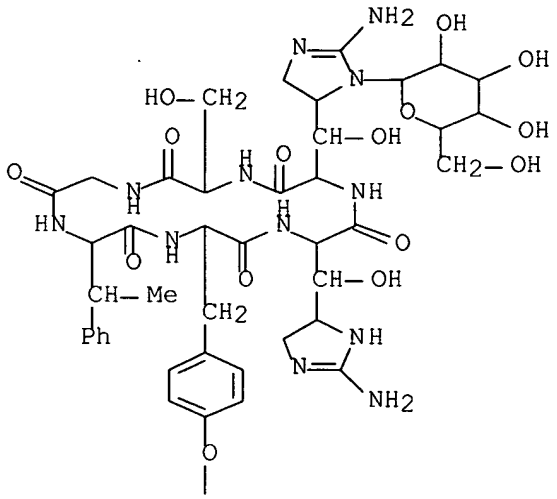
IT 473721-39-0P, AC 98-5 **473722-21-3P**, AC 98-1 473722-22-4P, AC 98-2 473722-23-5P, AC 98-3 473722-24-6P, AC 98-4
(substantially pure AC-98 glycopeptide antibiotics)

IT **473722-21-3P**, AC 98-1
(substantially pure AC-98 glycopeptide antibiotics)

RN 473722-21-3 USPATFULL

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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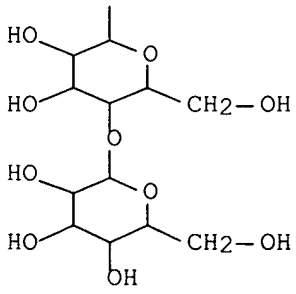


L26 ANSWER 2 OF 5 USPATFULL on STN

AN 2004:204143 USPATFULL Full-text

TI Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5

IN Carter, Guy Thomas, New City, NY, UNITED STATES
He, Haiyin, Washington Township, NJ, UNITED STATES

PA Wyeth Holdings Corporation, Madison, NJ, 07940 (U.S. corporation)

PI US 2004158035 A1 20040812
AI US 2004-771652 A1 20040204 (10)
RLI Division of Ser. No. US 2002-132012, filed on 25 Apr 2002, GRANTED, Pat. No. US 6713448
PRAI US 2001-286249P 20010425 (60) <--
US 2001-286244P 20010425 (60) <--
US 2001-286396P 20010425 (60) <--
DT Utility
FS APPLICATION
LREP WYETH, PATENT LAW GROUP, FIVE GIRALDA FARMS, MADISON, NJ, 07940
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 844
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides new substantially pure antibiotics designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 derived from the microorganism Streptomyces hygroscopicus.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5
PRAI US 2001-286249P 20010425 (60) <--
PRAI US 2001-286244P 20010425 (60) <--
PRAI US 2001-286396P 20010425 (60) <--
AB The invention provides new substantially pure antibiotics designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 derived from the microorganism Streptomyces hygroscopicus.
SUMM [0003] This invention relates to new substantially pure glycopeptide antibiotics, designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5, or pharmaceutically acceptable salts thereof, to methods for the preparation and isolation of such antibiotics,. . .
DRWD [0006] FIG. 1 shows the infrared absorption spectrum of **AC-98-1**
DRWD [0011] FIG. 6 shows the proton nuclear magnetic resonance spectrum of **AC-98-1**
DRWD [0016] FIG. 11 shows the carbon-13 nuclear magnetic resonance spectrum of **AC-98-1**
DETD [0021] New substantially pure glycopeptide antibiotics designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 or pharmaceutically acceptable salts thereof have now been found.
DETD [0022] The structure of **AC-98-1** is:
##STR1##
DETD [0023] The physico chemical characteristics of **AC-98-1** are as follows:
DETD [0063] In particular the structures of substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 are:
##STR6## ##STR7##
DETD [0064] This invention provides a method of preparing, separating and isolating substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from a recovered complex mixture.
DETD [0065] This invention further provides a method for preparing substantially pure glycopeptide antibiotic **AC-98-1** comprising the steps of:
DETD . . . strain of Streptomyces hygroscopicus in a suitable culture medium under aerobic conditions to produce a mixture of AC-98

antibiotics containing **AC-98-1**;

DETD [0067] b. recovering said mixture of AC-98 antibiotics containing **AC-98-1**; and

DETD [0068] c. separating and isolating substantially pure **AC-98-1** as the trifluoroacetic acid salt by reverse phase high pressure liquid chromatography with a mobile phase gradient of about 11%. . .

DETD [0090] It is understood that this invention encompasses all crystalline forms of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5. Further, substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 may be obtained as pharmaceutically acceptable salts which are those derived from such organic and. . .

DETD [0092] The present invention accordingly provides a pharmaceutical composition which comprises a substantially pure glycopeptide antibiotic **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 or a mixture thereof in combination or association with a pharmaceutically acceptable carrier. In particular, the present invention provides a pharmaceutical composition which comprises an effective amount of substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 or a mixture thereof and a pharmaceutically acceptable carrier.

DETD . . . bacterial infections in warm blooded animals which comprise administering to said animals an antibacterially effective amount of a substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 or a mixture thereof. Warm blooded animals includes humans.

DETD [0094] New substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 are obtained from a complex AC-98 antibiotic mixture which is produced by aerobic fermentation of. . .

DETD . . . collected as a AC-98 antibiotic mixture following washing with methanol and acetone. Separating the AC-98 antibiotic mixture into substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 is described in the present application.

DETD [0096] Experimental efforts showed that the AC-98 mixture could not be effectively separated into substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 using reverse phase HPLC on C-18 columns which included Dynamax and Phenomenex C-18 columns (60A. . . acid to control the acidity in the range of pH 3.5 and 5.5. The purification of the substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from the AC-98 antibiotic mixture is finally achieved by dissolving the AC-98 mixture in water. . .

DETD [0097] Separating the substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 each from the others is accomplished using reverse phase HPLC on a C18 column (YMC. . .

DETD [0098] Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 of this invention are defined as having, a purity of at least 85% when separated each from the others, as determined by high pressure liquid chromatography(HPLC). Preferably, substantially pure **AC-98-1** is obtained with a purity of at least 92%, substantially pure AC-98-2 is obtained with a purity of at least. . .

DETD [0099] The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 are isolated, purified and characterized from the AC-98 antibiotic mixture by dissolving the mixture in. . .

DETD . . . suitable culture medium is continued for about 24 to about 240

hours to produce a mixture of AC-98 antibiotics containing **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5. In particular, suitable liquid culture media are listed in Table A.

DETD [0109] Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 derive their utility from their antibacterial activity. In particular the substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 are active against methicillin-susceptible and methicillin-resistant strains of staphylococci, against penicillin-susceptible and penicillin-resistant streptococci, and. . .

DETD [0110] In therapeutic use, the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 of this invention may be administered in the form of conventional pharmaceutical compositions appropriate for. . . compositions may be formulated so as to be suitable for oral, parenteral or topical administration. The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 may be combined in admixture with a nontoxic pharmaceutical carrier, which carrier may take a. . .

DETD [0111] When the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 are employed for the above utility, they can be combined with one or more pharmaceutically. . . Such pharmaceutical preparations may contain, for example, from about 0.05 up to about 90% of the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 in combination with the carrier, more usually between about 5% and 60% by weight.

DETD [0112] An antibacterially effective amount of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 from about 0.5 mg/k body weight to about 200.0 mg/kg of body weight should be. . .

DETD [0113] Additionally, the antibacterially effective amount of the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 may be administered at a dosage and frequency without inducing side effects commonly experienced with. . . effects to normal tissues caused by administration at or above the antibacterially effective amount of the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5.

DETD [0116] These substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 may also be administered parenterally or intraperitoneally. Solutions or suspensions of these active compounds as. . .

DETD [0120] The mixture of AC-98 antibiotics is analyzed by HPLC to contain mainly five components, designated as **AC-98-1** (17%), AC-98-2 (19%), AC-98-3 (15%), AC-98-4 (29%), and AC-98-5 (4%). The relative quantity of each antibiotic is calculated based on. . .

DETD Substantially Pure Glycopeptide Antibiotics **AC-98-1**, AC-98-2, AC-98-3, and AC-98-4 from a Mixture of AC-98 Antibiotics

DETD . . . and upon evaporation infrared, proton nuclear magnetic resonance, and carbon 13 magnetic resonance spectra recorded. The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and a mixture as trifluoroacetate salts are isolated and listed in Table 1.

TABLE 1

COMPONENT	RETENTION TIME	WEIGHT COLLECTED*
Substantially Pure **AC-98-1** 35 mg	20 MINUTES	
Substantially Pure AC-98-2	28 MINUTES	29 mg
Substantially Pure AC-98-3	32 MINUTES	25 mg

Substantially Pure. . .

DETD [0129] The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 are tested in the following standard pharmacological test procedures.

DETD [0130] The in vitro antibacterial activity of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3 is determined against a spectrum of bacteria by a standard agar dilution method. Mueller-Hinton agar containing 5% sheep blood and two-fold decreasing concentrations of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3 are poured into petri dishes. The agar surfaces are inoculated. . . for that strain. The results are given in Table II.

Table II. In vitro antibacterial activity of substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3

TABLE II

In vitro antibacterial activity of substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3

Organism	MIC (mg/mL) **AC-98-1**	AC-98-2	AC-98-3	AC-98-4	AC-98-5
Staphylococcus aureus (NEMC-89-4)	>128	64	8	8	4
Staphylococcus aureus (ID-2371)	>128	128	8	8	4

Staphylococcus aureus (ID-2727). . .

DETD [0131] The in vivo antibacterial activity of substantially pure glycopeptides **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 is established by infecting female CD-1 mice from Charles River Laboratories, weighing 20+/-2 g each,. . . of water. The results of this test are given in Table III.

TABLE III

In vivo antibacterial activity of substantially pureglycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3

Compound	ED.sub.50 (iv, mg/kg) Staphylococcus aureus
AC-98-1	20
AC-98-2	>32
AC-98-3	3.8
AC-98-4	2.6
AC-98-5	0.6

CLM What is claimed is:

21. A method for preparing substantially pure glycopeptide antibiotic

AC-98-1 comprising the steps of: a. cultivating a suitable producing strain of Streptomyces hygroscopicus in a suitable culture medium under aerobic conditions to produce a mixture of AC-98 antibiotics containing **AC-98-1**; b. recovering said mixture of AC-98 antibiotics containing **AC-98-1**; and c. separating and isolating substantially pure **AC-98-1** as the trifluoroacetic acid salt by reverse phase high pressure liquid chromatography with a mobile phase gradient of about 11%. . .

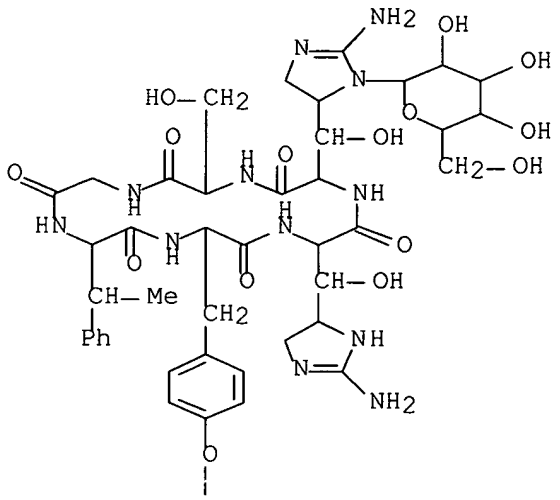
IT 473721-39-0P, AC 98-5 **473722-21-3P**, AC 98-1 473722-22-4P, AC 98-2 473722-23-5P, AC 98-3 473722-24-6P, AC 98-4
(substantially pure AC-98 glycopeptide antibiotics)

IT **473722-21-3P**, AC 98-1
(substantially pure AC-98 glycopeptide antibiotics)

RN 473722-21-3 USPATFULL

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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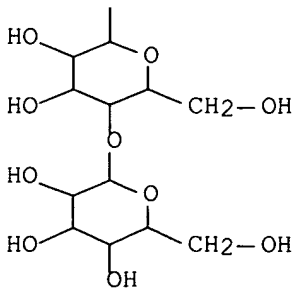


L26 ANSWER 3 OF 5 USPATFULL on STN
AN 2003:134523 USPATFULL Full-text
TI Glycopeptide antibiotics
IN Abbanat, Darren Robert, Cornwall, NY, UNITED STATES
Bailey, Arthur Emery, Bethel, CT, UNITED STATES
Bernan, Valerie Sue, New City, NY, UNITED STATES
Greenstein, Michael, Suffern, NY, UNITED STATES
Lotvin, Jason Arnold, Union, NJ, UNITED STATES
Ruppen, Mark Edward, Garnerville, NY, UNITED STATES
Sutherland, Alan Gordon, New City, NY, UNITED STATES
He, Haiyin, Washington Township, NJ, UNITED STATES
PA American Cyanamid Company, Madison, NJ (U.S. corporation)
PI US 2003092610 A1 20030515
US 6964860 B2 20051115
AI US 2002-131847 A1 20020425 (10)
PRAI US 2001-286396P 20010425 (60) <--
US 2001-286249P 20010425 (60) <--
US 2001-286244P 20010425 (60) <--
DT Utility
FS APPLICATION
LREP WYETH, PATENT LAW GROUP, FIVE GIRALDA FARMS, MADISON, NJ, 07940
CLMN Number of Claims: 105
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 18536
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides compounds of formula ##STR1##

Wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6a, R.sup.6b, R.sup.6c, R.sup.6d, R.sup.6e and R.sup.7 are defined in the specification. These compounds are useful as antibiotic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PRAI US 2001-286396P 20010425 (60) <--
PRAI US 2001-286249P 20010425 (60) <--
PRAI US 2001-286244P 20010425 (60) <--
SUMM . . . strain LL4600, the complex may also be prepared. Further separation of the complex of antibiotics by HPLC into individual components **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 and determination of the chemical structures by spectroscopy is described in copending provisional patent application. . . filed Apr. 25, 2001. The structures of the individual components are shown below.

R.sup.1 R.sup.2
R.sup.3 R.sup.4 R.sup.5

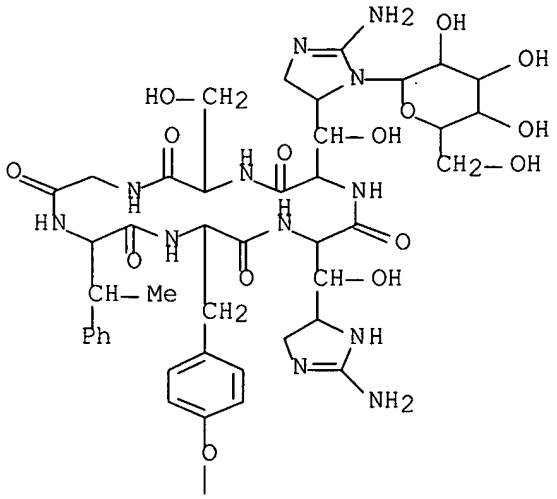
AC- 98-1 ##STR109## ##STR110##
OH OH ##STR111##

AC- 98-2 ##STR112## ##STR113##
OH OH ##STR114##

AC- 98-3 ##STR115## ##STR116##
OH OH ##STR117##

AC-. . .
IT 473721-39-0P, AC 98-5 **473722-21-3P**, AC 98-1 473722-22-4P, AC 98-2 473722-23-5P, AC 98-3 473722-24-6P, AC 98-4
(substantially pure AC-98 glycopeptide antibiotics)
IT **473722-21-3P**, AC 98-1
(substantially pure AC-98 glycopeptide antibiotics)
RN 473722-21-3 USPATFULL
CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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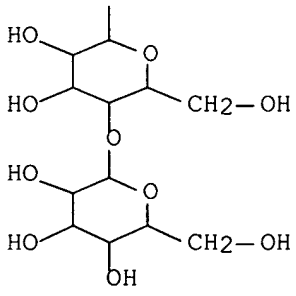


L26 ANSWER 4 OF 5 USPATFULL on STN
AN 2003:127597 USPATFULL Full-text
TI Glycopeptide antibiotics
IN Abbanat, Darren Robert, Cornwall, NY, UNITED STATES
Bernan, Valerie Sue, New City, NY, UNITED STATES
Dushin, Russell George, Garrison, NY, UNITED STATES
Greenstein, Michael, Suffern, NY, UNITED STATES

He, Haiyin, Washington Township, NJ, UNITED STATES
Lang, Stanley Albert, Carlsbad, CA, UNITED STATES
Newman, Howard, Monsey, NY, UNITED STATES
Sakya, Subas, East Lyme, CT, UNITED STATES
Sum, Phaik-Eng, Pomona, NY, UNITED STATES
Sutherland, Alan Gordon, New City, NY, UNITED STATES
Wang, Ting-Zhong, Spring Valley, NY, UNITED STATES
Lotvin, Jason Arnold, Union, NJ, UNITED STATES
Ruppen, Mark Edward, Garnerville, NY, UNITED STATES
Bailey, Arthur Emery, Bethel, CT, UNITED STATES
Cai, Ping, New City, NY, UNITED STATES
Shen, Bo, New berry Park, CA, UNITED STATES
Kong, Fangming, River Vale, NJ, UNITED STATES

PA American Cyanamid Company, Madison, NJ, UNITED STATES (U.S. corporation)
PI US 2003087812 A1 20030508
US 6914045 B2 20050705
AI US 2002-131890 A1 20020425 (10)
PRAI US 2001-286396P 20010425 (60) <--
US 2001-286249P 20010425 (60) <--
US 2001-286244P 20010425 (60) <--
DT Utility
FS APPLICATION
LREP Daniel B. Moran, Five Giralda Farms, Madison, NJ, 07940
CLMN Number of Claims: 128
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 18987
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides compounds of formula ##STR1##

Wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6a, R.sup.6b, R.sup.6c, R.sup.6d, R.sup.6e and R.sup.7 are defined in the specification. These compounds are useful as antibiotic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PRAI US 2001-286396P 20010425 (60) <--
PRAI US 2001-286249P 20010425 (60) <--
PRAI US 2001-286244P 20010425 (60) <--
SUMM . . . strain LL4600, the complex may also be prepared. Further separation of the complex of antibiotics by HPLC into individual components **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 and determination of the chemical structures by spectroscopy is described in copending provisional patent application. . . filed Apr. 25, 2001. The structures of the individual components are shown below.

R.sup.1 R.sup.2
R.sup.3 R.sup.4 R.sup.5

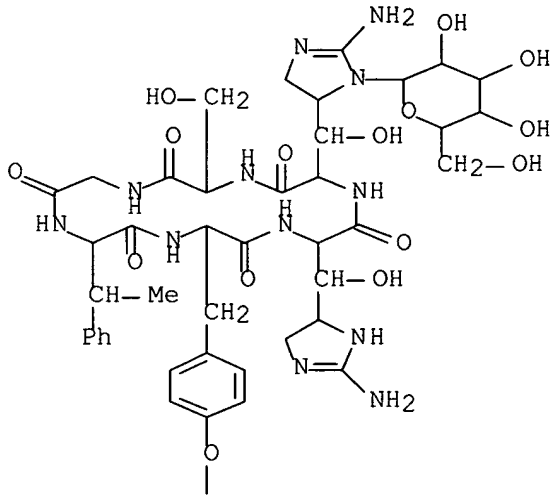
AC- 98-1 ##STR110## ##STR111##
OH OH ##STR112##

AC- 98-2 ##STR113## ##STR114##
OH OH ##STR115##

AC- 98-3 ##STR116## ##STR117##
OH OH ##STR118##

AC-. . .
IT 473721-39-0P, AC 98-5 **473722-21-3P**, AC 98-1 473722-22-4P, AC 98-2 473722-23-5P, AC 98-3 473722-24-6P, AC 98-4
(substantially pure AC-98 glycopeptide antibiotics)
IT **473722-21-3P**, AC 98-1
(substantially pure AC-98 glycopeptide antibiotics)
RN 473722-21-3 USPATFULL
CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

PAGE 1-A



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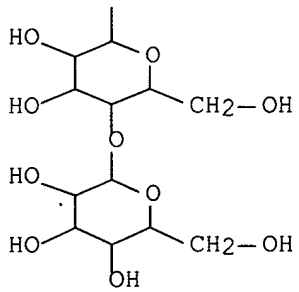

L26 ANSWER 5 OF 5 USPATFULL on STN
AN 2003:78588 USPATFULL Full-text
TI Substantially pure glycopeptide antibotics **AC-98-1**; AC-98-2; AC-98-3; AC-98-4 AND AC-98-5
IN Carter, Guy Thomas, New City, NY, UNITED STATES

He, Haiyin, Washington Township, NJ, UNITED STATES
PA American Cyanamid Company, Madison, NJ, UNITED STATES (U.S. corporation)
PI US 2003054508 A1 20030320
US 6713448 B2 20040330
AI US 2002-132012 A1 20020425 (10)
PRAI US 2001-286396P 20010425 (60) <--
US 2001-286244P 20010425 (60) <--
US 2001-286249P 20010425 (60) <--
DT Utility
FS APPLICATION
LREP Daniel B. Moran, Five Giralda Farms, Madison, NJ, 07940
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 835
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides new substantially pure antibiotics designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 derived from the microorganism Streptomyces hygroscopicus.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Substantially pure glycopeptide antibotics **AC-98-1**; AC-98-2; AC-98-3; AC-98-4 AND AC-98-5
PRAI US 2001-286396P 20010425 (60) <--
PRAI US 2001-286244P 20010425 (60) <--
PRAI US 2001-286249P 20010425 (60) <--
AB The invention provides new substantially pure antibiotics designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 derived from the microorganism Streptomyces hygroscopicus.
SUMM [0003] This invention relates to new substantially pure glycopeptide antibiotics, designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5, or pharmaceutically acceptable salts thereof, to methods for the preparation and isolation of such antibiotics,. . .
DRWD [0006] FIG. 1 shows the infrared absorption spectrum of **AC-98-1**
DRWD [0011] FIG. 6 shows the proton nuclear magnetic resonance spectrum of **AC-98-1**
DRWD [0016] FIG. 11 shows the carbon-13 nuclear magnetic resonance spectrum of **AC-98-1**
DETD [0021] New substantially pure glycopeptide antibiotics designated **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 or pharmaceutically acceptable salts thereof have now been found.
DETD [0022] The structure of **AC-98-1** is:
##STR1##
DETD [0023] The physico chemical characteristics of **AC-98-1** are as follows:
DETD [0067] In particular the structures of substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 are:
##STR6##
DETD [0068] This invention provides a method of preparing, separating and isolating substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from a recovered complex mixture.
DETD [0069] This invention further provides a method for preparing substantially pure glycopeptide antibiotic **AC-98-1** comprising the steps of:
DETD . . . strain of Streptomyces hygroscopicus in a suitable culture

medium under aerobic conditions to produce a mixture of AC-98 antibiotics containing **AC-98-1**;

DETD [0071] b. recovering said mixture of AC-98 antibiotics containing **AC-98-1**; and

DETD [0072] c. separating and isolating substantially pure **AC-98-1** as the trifluoroacetic acid salt by reverse phase high pressure liquid chromatography with a mobile phase gradient of about 11%. . .

DETD [0094] It is understood that this invention encompasses all crystalline forms of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5. Further, substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 may be obtained as pharmaceutically acceptable salts which are those derived from such organic and. . .

DETD [0096] The present invention accordingly provides a pharmaceutical composition which comprises a substantially pure glycopeptide antibiotic **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 or a mixture thereof in combination or association with a pharmaceutically acceptable carrier. In particular, the present invention provides a pharmaceutical composition which comprises an effective amount of substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 or a mixture thereof and a pharmaceutically acceptable carrier.

DETD . . . bacterial infections in warm blooded animals which comprise administering to said animals an antibacterially effective amount of a substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 or a mixture thereof. Warm blooded animals includes humans.

DETD [0098] New substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 are obtained from a complex AC-98 antibiotic mixture which is produced by aerobic fermentation of. . . collected as a AC-98 antibiotic mixture following washing with methanol and acetone. Separating the AC-98 antibiotic mixture into substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 is described in the present application.

DETD [0099] Experimental efforts showed that the AC-98 mixture could not be effectively separated into substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 using reverse phase HPLC on C-18 columns which included Dynamax and Phenomenex C-18 columns (60A. . . acid to control the acidity in the range of pH 3.5 and 5.5. The purification of the substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from the AC-98 antibiotic mixture is finally achieved by dissolving the AC-98 mixture in water. . .

DETD [0100] Separating the substantially pure **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 each from the others is accomplished using reverse phase HPLC on a C18 column (YMC. . .

DETD [0101] Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 of this invention are defined as having, a purity of at least 85% when separated each from the others, as determined by high pressure liquid chromatography(HPLC). Preferably, substantially pure **AC-98-1** is obtained with a purity of at least 92%, substantially pure AC-98-2 is obtained with a purity of at least. . .

DETD [0102] The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 are isolated, purified and characterized from the AC-98 antibiotic mixture by dissolving the mixture in. . .

DETD . . . suitable culture medium is continued for about 24 to about 240 hours to produce a mixture of AC-98 antibiotics containing **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5. In particular, suitable liquid culture media are listed in Table A.

DETD [0110] Substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 derive their utility from their antibacterial activity. In particular the substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and AC-98-5 are active against methicillin-susceptible and methicillin-resistant strains of staphylococci, against penicillin-susceptible and penicillin-resistant streptococci, and. . .

DETD [0111] In therapeutic use, the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 of this invention may be administered in the form of conventional pharmaceutical compositions appropriate for. . . compositions may be formulated so as to be suitable for oral, parenteral or topical administration. The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 may be combined in admixture with a nontoxic pharmaceutical carrier, which carrier may take a. . .

DETD [0112] When the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 are employed for the above utility, they can be combined with one or more pharmaceutically. . . Such pharmaceutical preparations may contain, for example, from about 0.05 up to about 90% of the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 in combination with the carrier, more usually between about 5% and 60% by weight.

DETD [0113] An antibacterially effective amount of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 from about 0.5 mg/kg of body weight to about 200.0 mg/kg of body weight should. . .

DETD [0114] Additionally, the antibacterially effective amount of the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5 may be administered at a dosage and frequency without inducing side effects commonly experienced with. . . effects to normal tissues caused by administration at or above the antibacterially effective amount of the substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 or AC-98-5.

DETD [0117] These substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 may also be administered parenterally or intraperitoneally. Solutions or suspensions of these active compounds as. . .

DETD [0121] The mixture of AC-98 antibiotics is analyzed by HPLC to contain mainly five components, designated as **AC-98-1** (17%), AC-98-2 (19%), AC-98-3 (15%), AC-98-4 (29%), and AC-98-5 (4%). The relative quantity of each antibiotic is calculated based on. . .

DETD Substantially Pure Glycopeptide Antibiotics **AC-98-1**, AC-98-2, AC-98-3, and AC-98-4 From a Mixture of AC-98 Antibiotics

DETD . . . and upon evaporation infrared, proton nuclear magnetic resonance, and carbon 13 magnetic resonance spectra recorded. The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4 and a mixture as trifluoroacetate salts are isolated and listed in Table 1.

TABLE 1

COMPONENT	RETENTION TIME	WEIGHT COLLECTED*
Substantially Pure **AC-98-1** 35 mg	20 MINUTES	
Substantially Pure AC-98-2	28 MINUTES	29 mg
Substantially Pure AC-98-3	32 MINUTES	25 mg
Substantially Pure AC-98-4	37 MINUTES. . .	

DETD [0130] The substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 are tested in the following standard pharmacological test procedures.

DETD [0131] The in vitro antibacterial activity of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3 is determined against a spectrum of bacteria by a standard agar dilution method. Mueller-Hinton agar containing 5% sheep blood and two-fold decreasing concentrations of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3 are poured into petri dishes. The agar surfaces are inoculated. . . concentration for that strain. The results are given in Table II.

TABLE II

In vitro antibacterial activity of substantially pure antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3

Organism	MIC (mg/mL) **AC-98-1**	AC-98-2	AC-98-3	AC-98-4	AC-98-5
Staphylococcus aureus (NEMC-89-4)	>128	64	8	8	4
Staphylococcus aureus (ID-2371)	>128	128	8	8	4
Staphylococcus aureus (ID-2727). . .					

DETD [0132] The in vivo antibacterial activity of substantially pure glycopeptides **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 is established by infecting female CD-1 mice from Charles River Laboratories, weighing 20+/-2 g each,. . . water. The results of this test are given in Table III.

TABLE III

In vivo antibacterial activity of substantially pure glycopeptide antibiotics **AC-98-1**, AC-98-2, AC-98-3, AC-98-4, and AC-98-5 from Examples 2 and 3

Compound	ED.sub.50 (iv, mg/kg) Staphylococcus aureus
AC-98-1	20
AC-98-2	>32
AC-98-3	3.8
AC-98-4	2.6
AC-98-5	0.6

CLM What is claimed is:

21. A method for preparing substantially pure glycopeptide antibiotic **AC-98-1** comprising the steps of: a.

cultivating a suitable producing strain of Streptomyces hygroscopicus in a suitable culture medium under aerobic conditions to produce a mixture of AC-98 antibiotics containing **AC-98-1**;
b. recovering said mixture of AC-98 antibiotics containing **AC-98-1**;and c. separating and isolating substantially pure **AC-98-1** as the trifluoroacetic acid salt by reverse phase high pressure liquid chromatography with a mobile phase gradient of about 11%. . .

IT 473721-39-0P, AC 98-5 **473722-21-3P**, AC 98-1 473722-22-4P, AC 98-2 473722-23-5P, AC 98-3 473722-24-6P, AC 98-4
(substantially pure AC-98 glycopeptide antibiotics)

IT **473722-21-3P**, AC 98-1
(substantially pure AC-98 glycopeptide antibiotics)

RN 473722-21-3 USPATFULL

CN Cyclo[glycyl-β-methylphenylalanyl-O-(4-O-α-D-mannopyranosyl-α-D-mannopyranosyl)tyrosyl-3-(2-amino-4,5-dihydro-1H-imidazol-4-yl)seryl-3-(2-amino-4,5-dihydro-1-α-D-mannopyranosyl-1H-imidazol-5-yl)serylseryl] (9CI) (CA INDEX NAME)

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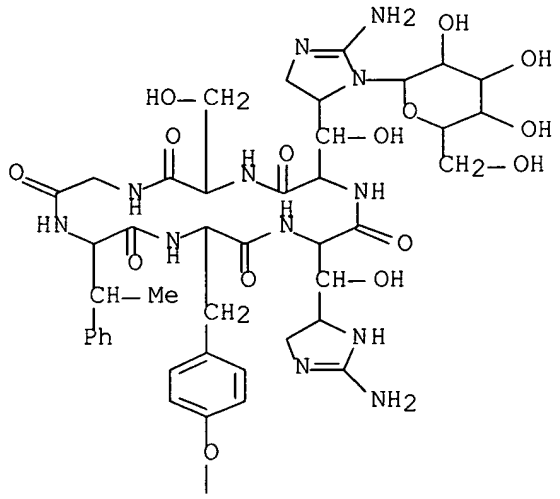
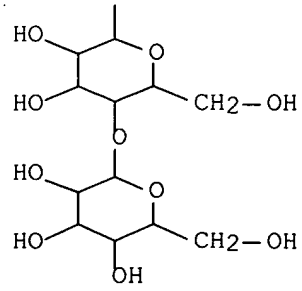


PAGE 2-A



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L3           106 S E3-E6
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L4           239 S E3
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L6             8 S E21
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